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10/577,620	01/29/2007	Maria Sitges Berrondo	251989	9639

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EXAMINER	
CARTER, KENDRA D	

ART UNIT	PAPER NUMBER
1627	

NOTIFICATION DATE	DELIVERY MODE
03/04/2010	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

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Office Action Summary	Application No.	Applicant(s)	
	10/577,620	SITGES BERRONDO ET AL.	
	Examiner	Art Unit	
	KENDRA D. CARTER	1627	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *29 December 2009*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-8* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-8* is/are rejected.

7)☒ Claim(s) *3* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *4/28/06* is/are: a)☐ accepted or b)☒ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

The Examiner acknowledges the applicant's remarks and arguments of December 23, 2009 made to the office action filed August 6, 2009. Claims 1-8 are pending and amended. The previous Non-Final office action is vacated and the NEW Non-Final office action is below. Particularly, the claim limitation of pharmaceutically acceptable vehicle was not clearly addressed, thus constituting a new office action.

In light of the amendments to the specification, the objection is withdrawn.

In light of the amendments the 35 U.S.C. 112, first paragraph rejections of claims 1 and 4-8 are withdrawn.

The Applicant's have stated that amendments were made to the drawings but they were not submitted. Thus the drawing objection is upheld.

In light of the claim amendments and addressing the pharmaceutically acceptable vehicle limitation, the previous 35 U.S.C. 103(a) rejection over Nekrassov er al. in view of Holtz et al. is withdrawn.

The Applicant's arguments are addressed below.

Drawings

The drawings are objected to under 37 CFR 1.83(a) because they fail to show what the asterisks stands for. Any structural detail that is essential for a proper understanding of the disclosed invention should be shown in the drawing. MPEP § 608.02(d). Corrected drawing sheets in compliance with 37 CFR 1.121(d) are required in reply to the Office action to avoid abandonment of the application. Any amended replacement drawing sheet should include all of the figures appearing on the immediate prior version of the sheet, even if only one figure is being amended. The figure or figure number of an amended drawing should not be labeled as "amended." If a drawing figure is to be canceled, the appropriate figure must be removed from the replacement sheet, and where necessary, the remaining figures must be renumbered and appropriate changes made to the brief description of the several views of the drawings for consistency. Additional replacement sheets may be necessary to show the renumbering of the remaining figures. Each drawing sheet submitted after the filing date of an application must be labeled in the top margin as either "Replacement Sheet" or "New Sheet" pursuant to 37 CFR 1.121(d). If the changes are not accepted by the examiner, the applicant will be notified and informed of any required corrective action in the next Office action. The objection to the drawings will not be held in abeyance.

Claim Objections

Claim 3 is objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form. Particularly, claim 3 is the same as claim 2.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was

not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1-8 are rejected under 35 U.S.C. 103(a) as being unpatentable over Nekrassov et al. (Brain Research, 2000, vol. 868, pp. 222-229) in view of Holtz et al. (Eur. Arch Otorhinolaryngol, 1990, vol 247, pp. 202-205) and Tigyi et al. (US 4,882,336)

Nekrassov et al. teach vinpocetine protects from aminoglycoside antibiotic-induced hearing loss in guinea pig in vivo (see title). Amikacin, the aminoglycoside antibiotic, increases the auditory brainstem response (ABR) at 4 and 8 kHz, but when vinpocetine is administed by i.p. at 2 mg/kg for 13 days after administration of Amikacin, the increase ABR threshold is reduced (see abstract and page 225, section 3.5; addresses claims 1, 2 and 4-8) in the first and later waves (i.e. P1, P3 and P4 in fig. 1; addresses claims 2 and 3).

Nekrassov et al. do not teach that the hearing loss is associated with epilepsy (claim 1), nor the specific treatment of alterations of retro-cochlear origin characterized by the inhibition of the alterations of the ABR (claim 2). Nekrassov et al. also does not specifically teach vinpocetine is in an amount effective to inhibit the epileptic cortical activity for ictal and post-ictal periods (claim 4). Nekrassov et al. also does not specifically teach a pharmaceutically acceptable vehicle (claim 1).

Holtz et al. teach that aminoglycoside therapy causes cochlear and retrocochlear changes in the auditory pathways (see page 205, column 1, lines 2-5).

Tigyi et al. teach that ethyl apovincaminate (i.e. vinpocetine) can be administered parenterally with suitable carriers (see column 5, lines 25-35 and 55-60).

To one of ordinary skill in the art at the time of the invention would have found it obvious and motivated to combine the teachings of Nekrassov et al. and that the hearing loss is associated with epilepsy as in claim 1 because Nekrassov et al. teach the treatment and prevention of hearing loss at 4 and 8 kHz with the Applicant's claimed compound. Thus, regardless of the cause, hearing loss is still treated. One would be motivated to try a treatment for hearing loss regardless of its cause, especially if the hearing loss was treated.

To one of ordinary skill in the art at the time of the invention would have found it obvious and motivated to combine the teachings of Nekrassov et al. and treatment of alterations of retro-cochlear origin characterized by the inhibition of the alterations of the ABR (claims 2 and 3) because Nekrassov et al. teach that the ABR waves were inhibited by the same compound. Further, Holtz et al. teach that aminoglycoside therapy causes retro-cochlear changes in auditory pathways. Thus, the treatment of Nekrassov et al. is treating alterations of retro-cochlear origin characterized by the

inhibition of the alterations of the amplitudes and latencies of the later waves of the ABR.

To one of ordinary skill in the art at the time of the invention would have found it obvious and motivated to combine the teachings of Nekrassov et al. and a pharmaceutically acceptable vehicle because Nekrassov et al. teach that vinpocetine can be administered parenterally, and Tigyi et al. teach that ethyl apovincaminate (i.e. vinpocetine) can be administered parenterally with suitable carriers (see column 5, lines 25-35 and 55-60). Thus, it is known in the art to formulate vinpocetine with pharmaceutically acceptable vehicles.

To one of ordinary skill in the art at the time of the invention would have found it obvious and motivated to combine the teachings of Nekrassov et al. and that vinpocetine is in an amount effective to inhibit the epileptic cortical activity for ictal and post-ictal periods (claim 4) because Nekrossov et al. teach that vinpocetine was administered at 2 mg/kg, which is the effective amount disclosed in the specification (see page 5, paragraph 23, last line). Thus, the same compound at the same amount would be in an effective amount to inhibit the epileptic cortical activity for ictal and post-ictal periods.

Response to Arguments

Applicant's arguments have been fully considered but they are not persuasive.

> The Applicant's argues that the aminoglycoside studies of Nekrossov et al. and Hotz et al. invariable involve alterations in the most peripheral generators of the first wave of the ABR. While aminoglycoside-induced changes in the first wave may indirectly affect other ABR waves, the reverse is not true for ABR wave alterations associated with epilepsy, i.e., changes in the later ABR waves associated with epilepsy cannon indirectly change the first wave, which originates in peripheral structures. The prior art does not teach a method for treating epilepsy-induced hearing loss with an acute vinpocetine pre-treatment. The Applicant further argues that the Examiner can not use hindsight reconstruction to pick and choose among isolated disclosures in the prior art to deprecate the claimed invention.

The Examiner disagrees because first the claims are drawn to the treatment and prevention of hearing loss associated with epilepsy. Second, as the stated in the new rejection above, when vinpocetine is administered by i.p. at 2 mg/kg for 13 days after administration of Amikacin, the increase ABR threshold is reduced (see abstract and page 225, section 3.5) in the first and later waves (i.e. P1, P3 and P4 in fig. 1; addresses claims 2 and 3). In response to applicant's argument that the examiner's conclusion of obviousness is based upon improper hindsight reasoning, it must be recognized that any judgment on obviousness is in a sense necessarily a reconstruction based upon hindsight reasoning. But so long as it takes into account only knowledge which was within the level of ordinary skill at the time the claimed invention was made, and does not include knowledge gleaned only from the applicant's disclosure, such a

reconstruction is proper. See *In re McLaughlin*, 443 F.2d 1392, 170 USPQ 209 (CCPA 1971).

Conclusion

No claims allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to KENDRA D. CARTER whose telephone number is (571)272-9034. The examiner can normally be reached on 9:00 am - 5:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sreeni Padmanabhan can be reached on (571) 272-0629. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Kendra D Carter/
Examiner, Art Unit 1627

/SREENI PADMANABHAN/
Supervisory Patent Examiner, Art Unit 1627